

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Michel PAIRET et al. :

Serial No.: 10/776,757 : Examiner: Barbara P. Badio

Filed: February 11, 2004 : Group Art Unit: 1628

For: PHARMACEUTICAL COMPOSITIONS BASED ON
ANTICHOLINERGICS AND CORTICOSTEROIDS

REPLY BRIEF UNDER 37 C.F.R. §41.41

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Sir:

This Reply Brief is submitted under 37 C.F.R. §41.41 in response to the Examiner's Answer, mailed December 21, 2010. Appellants maintain their reliance upon their Brief filed October 4, 2010. The following points are made for emphasis or clarification of points made in the Brief in light of the comments thereon in the Examiner's Answer and/or are made in response to new points of argument raised in the Examiner's Answer.

1) The Examiner's Answer, as a whole, essentially fails to address a key point made in Appellants' Brief. The claims on appeal are drawn to a very specific combination of a tiotropium component, a specific ciclesonide steroid component and specific excipients. As pointed out in the Brief (paragraph bridging pages 7-8 and page 13, first full paragraph), none of the cited references disclose a composition which specifically uses a ciclesonide steroid component. No objective reasoning is provided for why one of ordinary skill in the art would select ciclesonide specifically for compositions according to the claimed invention when none of the references disclose using ciclesonide for any composition.

2) In the Examiner's Answer (page 8, second full paragraph, and elsewhere), in response to appellants' arguments that Nishimura discloses only an additive effect for its combination and thus the synergistic result shown for appellants' invention is unexpected, the

Examiner alleges that non-obviousness can only be shown by providing a direct comparison to the closest prior art. Appellants respectfully submit that the Examiner's position is legally incorrect. As pointed out with supporting case cites in the paragraph bridging pages 4-5 of Appellants' Brief "all evidence of nonobviousness must be considered when assessing patentability" and that a showing of a synergistic effect of a combination alone can be sufficient proof of nonobviousness. In making this argument, the Examiner's Answer, thus, fails to address appellants' relevant point, i.e., that the synergistic result is clearly unexpected. Not only is it unexpected, it is directly contrary to Nishimura's indication that only an additive effect is obtained with its distinct combination. That the Examiner erroneously alleges that another test should be provided does not refute the clear unexpected nature of the showing appellants have made on the record. The Examiner even agrees (top of page 10 of Examiner's Answer) that appellants' showing provides a clear case for synergistic results.

3) It is alleged in the Examiner's Answer (e.g., page 9, last paragraph) that appellants' are arguing based on an incorrect comparison of data from experiments on dogs versus data from Nishimura of experiments on humans. The record will confirm and appellants clearly pointed out in the Brief (page 6, first paragraph) that they never alleged any comparison of their data to the human data from Nishimura. Appellants' arguments regarding Nishimura are that it fails to suggest that its combination would provide a synergistic effect and, thus, appellants' showing of a synergistic effect is unexpected. The showing of synergism in the declaration is based only on appellants' own data in the 37 C.F.R. §1.132 Declaration from experiments with dogs, where all of the experiments are in a side-by-side manner. Appellants rely only on the data in their declaration for this comparison. The declaration compares the combination composition according to the invention versus the additive effect of the components separately; i.e., the classic and accepted way of showing synergism.

4) It is alleged in the Examiner's Answer (e.g., page 10, second paragraph) that the generic combination of an anticholinergic and a steroid is taught by Nishimura and that appellants have not provided any evidence to show that such generic combination would provide unobvious or unexpected results when compared to the Nishimura composition. Appellants submit that this is not irrelevant to the issues on appeal. The generic combination of an anticholinergic and a steroid is not the subject of the invention. As argued throughout appellants' Brief, the invention is based on the discovery that the specific combination of the

particular tiotropium anticholinergic and particular ciclesonide steroid gives an unexpected synergistic result. Such is clearly unexpected in view of Nishimura's teaching that only an additive effect would be expected and in view of the other cited references considered as a whole. Additionally, Nishimura does not provide such a broad generic teaching; it teaches the specific combination of an oxitropium anticholinergic and a beclomethasone steroid.

5) The Examiner's Answer provides an argument not previously made in the paragraph bridging pages 10-11. The Examiner alleges that appellants' showing is not commensurate in scope with the claims because the declaration allegedly suggests that the synergistic effect is dependent on the dose of the components and the claims do not recite such specified dose. Appellants respectfully disagree that the declaration suggests that the synergism effect is dependent on the dose. The declaration merely states that the synergism that is shown was with a lower tiotropium dose. The declarant gives no indication that the effect would only be observed at lower doses. To the contrary, the declarant's broader conclusion in the sentence immediately before the one quoted in the Examiner's Answer (see page 4, fifth paragraph, of the declaration) is that the combination – without limitation on the dose – clearly resulted in synergistic bronchoprotection. The following sentence regarding the lower dose merely points out that the synergistic effect is of particular significance when looking at the lower dose. This is because that is a key advantage of obtaining a synergistic effect. Getting such a super-additive effect is particularly advantageous because it allows one to use lower doses of the actives and lessen other possible undesired effects of the drugs.

6) The Examiner's counterargument regarding the excipient (page 11, first full paragraph) is only relevant when considering Keller. Thus, this counterargument does not apply to the first grounds of rejection not relying on Keller. In any event, the nonobviousness of the claimed invention is shown for the combination of actives regardless of whether Keller is combined.

7) It is alleged in the Examiner's Answer (paragraph bridging pages 11-12) that Nishimura supports a reasonable expectation by one of ordinary skill in the art of obtaining an improved treatment when making any combination of an anticholinergic and a steroid. This is similar to the point 4) addressed above. The allegation is clearly not supported by Nishimura, which is directed only to a specific combination of an oxitropium anticholinergic and a beclomethasone steroid. Further, the allegation does not address appellants' key point that the improvement alleged by Nishimura is only additive, while appellants have

surprisingly shown a synergistic (i.e., super-additive) effect for the specific claimed combination. Synergism is clearly an unexpected result when the reference explicitly states only an additive effect.

For the above reasons and the reasons set forth in Appellants' Brief, it is submitted that the decision of the Examiner finally rejecting claims 3, 4, 9, 10, 15-17, 19-21, 23, 25, 26, 31-37, 39 and 63-66, on appeal, is in error and should be reversed.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

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